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Analysis of pH in Blood Plasma at Steady State in Vivo

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ABSTRACT

pH in blood plasma depends not only on Pco_2, but also on the bicarbonate concentration ($[HCO_3^-]$). $[HCO_3^-]$ has a Pco_2-dependent respiratory component ($[HCO_3^-]^*$), and a Pco_2-independent metabolic component ($[HCO_3^-]^o$). $[HCO_3^-]^*$ can be approximated by a defined exponential function of Pco_2. When $[HCO_3^-]^o = 0$, let $[H^+]$ and pH be designated by $[H^+]^*$ and pH*, respectively. At any value of Pco_2, the deviation of pH* from 7.4 (pH*−7.4) is given by the Henderson equation as a linear function of log Pco_2. At a given Pco_2, the difference between pH and pH* (pH−pH*) at any $[HCO_3^-]^o$ is given by the common logarithm of the ratio ($[HCO_3^-]/[HCO_3^-]^*$). The effects of Pco_2 and $[HCO_3^-]^o$ on acid-base balance can be accurately analysed by using the equatons for pH*−7.4 and pH−pH*, derived from the Henderson equation, together with the exponential function of Pco_2 for $[HCO_3^-]^*$. The use of the equation in defining acid-base status is illustrated here by application to results from elderly patients and healthy volunteers.

Key words : Acid-base balance, Logarithmic transformation, Ratio of $[H^+]$, Henderson equation, Components of $[HCO_3^-]$

INTRODUCTION

pH is the logarithm of the H^+ concentration ($[H^+]$). $[H^+]$ in blood plasma is proportional to the ratio of Pco_2 to the bicarbonate concentation, $[HCO_3^-]$, as given by the Henderson equation[1]. $[HCO_3^-]$ has a Pco_2-dependent respiratory component ($[HCO_3^-]^*$) and a Pco_2-independent metabolic component ($[HCO_3^-]^o$). In a preceding paper[2], it was shown that $[HCO_3^-]^*$ could be approximated by a defined

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exponential functuion of Pco_2[2]. Designating $[H^+]$ and pH, at the standard state of $[HCO_3^-]^o = 0$, as $[H^+]^*$ and pH*, respectively, $[H^+]^*$ was also approximated by a defined exponential function of Pco_2 from the Henderson equation and Pco_2 at pH=7.4 was easily derived as 42.6 mmHg. From the ratio of $[H^+]^*$ at any Pco_2 to that at Pco_2=42.6 mmHg, the relationship between Pco_2 and pH*−7.4 was also simply derived from the ratio Pco_2/42.6. When $[HCO_3^-]^o$ changes from zero to any other level without a change in Pco_2, the difference between pH and pH* (pH−pH*) is always equal to the logarithm of the ratio $[HCO_3^-]/[HCO_3^-]^*$. In measured data the deviation of pH from 7.4 has been considered as comprising two pH differences, pH−pH* and pH*−7.4, whose values have been precisely calculated through the mathematical formulae. The validity of this method has been demonstrated in a number of measured data.

METHODS

The relationship between Pco_2 and pH−7.4.*

The relationship of Pco_2 to pH was introduced to analyse changes in pH. In a foregoing paper[2], $[HCO_3^-]^*$ was given by the following exponential function of Pco_2:

$$[HCO_3^-]^* = 4.717\ Pco_2^{0.457}, \text{(mEq)}. \quad (1)$$

Combining Eq. (1) with the Henderson equation, the following equation is now derived:

$$[H^+]^* = (24.465/4.717)\ Pco_2^{0.543}, \text{(nEq)}. \quad (2)$$

$[H^+]$ at pH = 7.4 is approximately 39.81 nEq. Pco_2 at pH = 7.4, evaluated from Eq. (2), is about 42.6 mmHg. The ratio of $[H^+]^*$ at any Pco_2 to that at Pco_2 = 42.6 mmHg is given from Eq. (2) by

$$[H^+]^*/39.81 = (Pco_2/42.6)^{0.543}. \quad (3)$$

Taking the logarithm of both sides of Eq. (3), the following equation is obtained:

$$pH^* - 7.4 = -0.543 \log(Pco_2/42.6) \quad (4)$$

Figure 1 shows pH*−7.4 plotted against Pco_2. This difference becomes zero at Pco_2 = 42.6 mmHg and increases with a decrease in Pco_2, and *vice versa*.

The relationship between pH−pH and $[HCO_3^-]/[HCO_3^-]^*$.* $[HCO_3^-]^o$ usually changes from zero to any other level without a change in Pco_2. That is, $[HCO_3^-]$ changes from $[HCO_3^-]^*$ to the measured level, where $[HCO_3^-] = [HCO_3^-]^* + [HCO_3^-]^o$, without a change in Pco_2. According to the change in $[HCO_3^-]^o$, $[H^+]$ also changes from $[H^+]^*$ to the measured $[H^+]$ level. Since there is no change in Pco_2 in this case, the ratio of the measured $[H^+]$ to $[H^+]^*$ is given from the Henderson

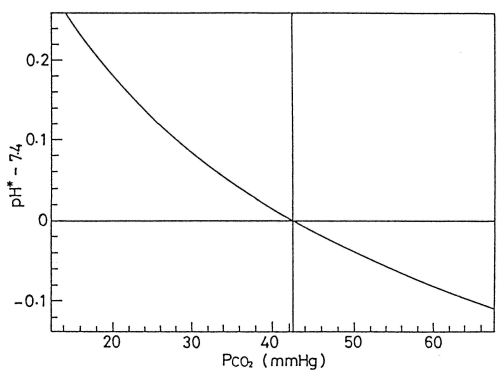

Fig. 1.
pH*−7.4 plotted against Pco_2

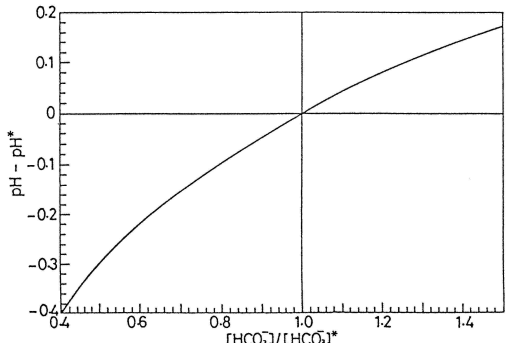

Fig. 2.
pH−pH* plotted against the ratio, $[HCO_3^-]/[HCO_3^-]^*$

Table 1. A flow chart of the Excel program for analysing the difference in pH

A	B	C
Name	C 2	
Age	C 3	
Date	C 4	
pH	C 5	
Pco_2	C 6	
pH−7.4	C 7	C5−7.4
$[H^+]$	C 8	=10^(9−C5)
$[HCO_3^-]$	C 9	=24.465*C6/C8
$[HCO_3^-]^*$	C10	=4.717*C6^0.457
$[HCO_3^-]/[HCO_3^-]^*$	C11	=C9/C10
pH−pH*	C12	=LOG10(C11)
$Pco_2/42.6$	C13	=C6/42.6
pH*−7.4	C14	=−0.543*LOG10(C13)

equation as

$$[H^+]^*/[H^+]=([HCO_3^-]^*+[HCO_3^-]^\circ)/[HCO_3^-]^*, = [HCO_3^-]/[HCO_3^-]^*. \quad (5)$$

Taking the logarithm of Eq. (5), we obtain the following equation:

$$pH-pH^*=\log([HCO_3^-]/[HCO_3^-]^*). \quad (6)$$

Figure 2 shows pH−pH* plotted against the ratio $[HCO_3^-]/[HCO_3^-]^*$.

Subjects and biochemical analysis. To verify the validity of the equations for pH differences, pH and Pco_2 were measured (Ciba Corning 188) in patients with acid-base disorders aged from 67 to 98 years and in healthy volunteers aged from 19 to 55 years. The values for the components of the deviation of pH from 7.4, i.e. pH*−7.4 and pH−pH* were calculated using Eqs. (4) and (6), respectively. At a later stage of this study, the calculation was facilitated by using an Excel computer program on a

Table 2. Analysed data from four patients, characterizing the four groups of measured pH values

Group	1	2	3	4
Name & Sex	MM(F)	KO(M)	YM(M)	KT(F)
Age	78	87	80	81
Date	950417	931026	921105	930421
pH	7.246	7.293	7.513	7.454
Pco_2(mmHg)	18.9	52.5	33.1	60.6
pH−7.4	−0.154	−0.107	0.113	0.054
$[H^+]$(nEq)	56.754	50.933	30.690	35.156
$[HCO_3^-]$ (mEq)	8.147	25.218	26.386	42.171
$[HCO_3^-]^*$ (mEq)	18.072	28.826	23.347	30.779
$[HCO_3^-]/[HCO_3^-]^*$	0.451	0.875	1.130	1.370
pH−pH*	−0.346	−0.058	0.053	0.137
$Pco_2/42.6$	0.444	1.232	0.777	1.423
pH*−7.4	0.192	−0.049	0.060	−0.083

Table 3. Summarized data on the analysis of pH −7.4 in elderly patients

Group	1	2	3	4
$[HCO_3^-]$ (mEq)	$<[HCO_3^-]^*$	$<[HCO_3^-]^*$	$>[HCO_3^-]^*$	$>[HCO_3^-]^*$
Pco_2 (mmHg)	<42.6	>42.6	<42.6	>42.6
No of subjects	37	24	22	42
Mean age & SD	81.8 + 8.1	85.3+6.8	85.6+5.6	85.7+5.9
No of samples	47	26	64	49
pH−pH*	−0.104+0.064	−0.066+0.032	0.087+0.127	0.100+0.032
pH*−7.4	0.073+0.054	−0.032+0.022	0.032+0.023	−0.037+0.027
pH −7.4	−0.031+0.057	−0.098+0.035	0.119+0.034	0.063+0.035

Table 4. Summarized data on the analysis of pH−7.4 in volunteers

Group	1	2	3	4
$[HCO_3^-]$ (mEq)	$<[HCO_3^-]^*$	$<[HCO_3^-]^*$	$>[HCO_3^-]^*$	$>[HCO_3^-]^*$
Pco_2 (mmHg)	<42.6	>42.6	<42.6	>42.6
No of subjects	14	18	3	32
Mean age & SD	38.9+11.3	29.0+8.4	46.0+7.3	32.4+9.7
No of samples	14	18	3	32
pH−pH*	−0.012+0.007	−0.010+0.009	0.014+0.010	0.017+0.009
pH*−7.4	0.018+0.012	−0.026+0.018	0.004+0.002	−0.037+0.023
pH −7.4	0.006+0.015	−0.036+0.022	0.018+0.008	−0.020+0.024

personal computer (DELL). The flow chart of the program is shown in Table 1.

RESULTS

Analysed data were divided into four groups according to the plus or minus sign of pH−pH* and pH*−7.4. Table 2 shows data calculated from four typical patients *via* the computer, each characteristic one of the four groups. pH−pH* was negative, or acidotic in Group 1 and 2, whereas in Group 3 and 4, pH−pH* was positive, or alkalotic. In Group 1 and 3, Pco_2 was lower than 42.6 mmHg and pH*−7.4 became positive, while in Group 2 and 4, Pco_2 was higher than 42.6 mmHg and pH*−7.4 was negative. The sign of pH−pH* in Group 1 and 4 was opposite to that of pH*−7.4, while in Group 2 and 3 the sign of pH−pH* was the same as that of pH*−7.4. Therefore, in Group 1, the value of pH−7.4 became less negative than pH−pH*. In Group 2, pH*−7.4 was negative, hence, pH−7.4 became more negative than pH−pH*. Pco_2 in Group 3 was lower than 42.6 mmHg and pH*−7.4 became positive, while in Group 4 Pco_2 was higher than 42.6 mmHg and pH*−7.4 became negative. Hence, in Group 3, pH−7.4 was more positive than pH−pH*, while in Group 4, pH−7.4 was less positive than pH−pH*. The effect of Pco_2 on pH is clearly seen in these data.

Summarized data for the analysis of pH−7.4 in elderly patients are shown in Table 3. In acidotic blood of Group 1 (n = 47) the pH-compensating effect of Pco_2 was observed. In Group 2 (n = 26), however, Pco_2 was higher than 42.6 mmHg and no effect to compensate pH was observed, making pH−7.4 much more negative than pH−pH*. In alkalotic blood in Group 4 (n = 49) Pco_2 was higher than 42.6 mmHg and pH*−7.4 became negative. Hence,

the effect of Pco_2 compensating pH−pH* was observed. In Group 3 (n = 64), however, Pco_2 was lower than 42.6 mmHg, pH*−7.4 became positive, and no pH-compensating effect appeared. By comparing the mean and SD values of pH−7.4 between Groups 1 and 2 and those between Groups 3 and 4, it is apparent that the effect of Pco_2 compensating pH−pH* was statistically significant ($P<0.01$).

Table 4 shows the summarized data for the analysis of pH−7.4 in the volunteers. Because blood gas was analysed only in venous samples, the range of Pco_2 and the size of pH*−7.4 in Group 4 of Table 4 were almost the same as those shown in Table 3. However, other values for the pH differences in Table 4 were all smaller than those in Table 3. Since Eq. (1) is the exponential function of Pco_2, all the pH values was calculated *via* the logarithmic functions of Pco_2 and $[HCO_3^-]$, and therefore, the relationship between pH−pH*, pH*−7.4 and pH−7.4 became relevant irrespective of the size of the pH difference .

DISCUSSION

$[H^+]$ in blood is defined by Pco_2 and $[HCO_3^-]$ as given by the Henderson equation. As stated in the Introduction $[HCO_3^-]$ has the respiratory and metabolic components. Similarly to $[HCO_3^-]$, pH also has a Pco_2-dependent respiratory component (pH*) and a Pco_2-independent metabolic component. The latter component has hitherto been assessed by obtaining $[HCO_3^-]^o$ at 40 mmHg Pco_2, i.e. base excess (BE)[3] mainly by using the CO_2 dissociation curve measured in oxygenated blood *in vitro*. At steady state *in vivo*, a change in $[HCO_3^-]$ occurs together with the change in O_2-saturation. Therefore, the change in $[HCO_3^-]$ always implys the Haldane effect, making the relationship between Pco_2 and $[HCO_3^-]$ at steady state *in vivo* different from that measured in oxygenated blood *in vitro*. Recently, we could approximate $[HCO_3^-]^*$ with an exponential function of Pco_2[2]. Moreover, the validity of the function was verified by comparing it with the similar function obtained from CO_2 reaction rates *via* the Michaelis-Menten equation for carbonic anhydrase[4]. Thus, $[HCO_3^-]^o$ can now be accurately obtained by subtracting $[HCO_3^-]^*$ from the measured $[HCO_3^-]$ value.

Basically, the dimension of pH is different from that of Pco_2 and $[HCO_3^-]$. It is impossible to express pH by using a relevant mathematical formula without converting the dimensions of Pco_2 and $[HCO_3^-]$. In the present study, we have converted these dimensions by taking the ratio of the parameter values at two different Pco_2 levels. Since $[H^+]$ at pH = 7.4 is about 39.81 nEq, the ratio $[H^+]/39.81$ was introduced in place of $[H^+]$. Since $[H^+]/39.81$ is dimensionless, the dimension of $[H^+]$ (nEq) turned naught by taking the ratio. The logarithm of $[H^+]/39.81$ is equal to 7.4−pH, therefore, the dimension of 7.4−pH becomes different from that of pH. Since $[HCO_3^-]^*$ was given by the exponential function of Pco_2, the ratio $Pco_2/[HCO_3^-]^*$ was also given by an exponential function of Pco_2. As shown by the Henderson equation, since there is a proportional relationship between $[H^+]^*$ and the ratio $Pco_2/[HCO_3^-]^*$, Pco_2 at pH = 7.4 was evaluated to be 42.6 mmHg. Finally, Eq. (4) demonstrates that pH*−7.4 was given by a defined proportional function of log (Pco_2/42.6). Hence, the chemicophysical property that $[HCO_3^-]^*$ was approximated by the exponential function of Pco_2 is essential for the present pH analysis.

Hitherto, the base excess (BE)[3] has been estimated from measured data for pH and Pco_2 using the Henderson equation. However, even where BE is known, the accurate relationship between BE and the metabolic change in pH will not be obtained. Hence, the use of the exponential function of Pco_2 for $[HCO_3^-]^*$, such as Eq. (1), is of great value for quantifying the acid-base status.

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